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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/682,303 | 10/09/2003 | Raul Trillo | ANA 5955 (61834) | 7332 |

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| EXAMINER | |
|---|---|
| WILLIAMS, LEONARD M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/682,303 | TRILLO ET AL. | |
| | Examiner | Art Unit | |
| | Leonard M. Williams | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2,4,5 and 7-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-5, and 7-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

***Response to Amendment***

The amendment filed 09/10/2007 amending claim 1 to include the phrase "a sub-anesthetic" amount and adding new claim 13 has been entered. Claims 3 and 6 have been cancelled. Claims 1-2, 4-5 and 7-13 are currently pending.

Applicant's arguments filed 09/10/2007 have been fully considered but they are not persuasive. The applicant's have amended claim 1 to specify that the amount of halogenated volatile anesthetic is "sub-anesthetic". In the remarks the applicant's have argued, on pages 4-5, that the insertion of this language overcomes the prior art due to the fact that Saito et al. indicate that the protective benefits may be due to cerebrovascular and electrophysiologic influences. The applicant further asserts that Saito et al. suggest that the protective effect may stem from suppression of neuronal activity. The applicant's have interpreted the idea of suppression of neuronal activity means the anesthetic effect. The examiner respectfully disagrees with the applicants assertions. Saito et al. discloses many possible reasons for the activity seen, there is no particular reason to assume that if Saito et al. even supposes that the activity is potentially due to the anesthetic effect there is no evidence that Saito et al. believes this is the only pathway or activity possible. Further the applicant's argue that there is no reason to assume that just because activity is seen in the brain that any other organ would be protected by the application of the HVA. The examiner respectfully disagrees.

The presumption of this assertion is that the protective effect is due only to the anesthetic effect of the HVA administered and that this is the sole reason why there is protective activity in the brain (which is not indicated nor supported by Saito et al.). Even if this was the case, the HVA administered would still inherently be treating the conditions currently claimed by applicant. Further new claim 13 limits the tissue to heart tissue. The examiner respectfully points out that this does not overcome the prior art as applied. The fact that Saito et al. demonstrated activity in the brain indicates that equivalent activity should be seen in other organs suffering from equivalent disorders (ischemia-reperfusion). The sub-anesthetic dosing of the HVA is easily within the ability of one of ordinary skill in the art and one of ordinary skill in the art would seek to adjust the amount of HVA in the treatment of a condition other than anesthesia in order to limit the potential side-effects of HVA at anesthetic levels.

For the reasons detailed above and for the reasons of record the rejections of the last office are maintained but modified to include new claim 13. This action is made final. The modified rejections are included below.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al. (Reduction of Infarct Volume by Halothane: Effect on Cerebral Blood Flow or Perifocal Spreading Depression-Like Depolarizations, Journal of Cerebral Blood Flow and Metabolism, 1997, vol. 17, pp 857-864) in view of Gray et al. (GB2350297).

Saito et al. teach, in the abstract, that when halothane was given to cats with induced permanent focal ischemia via left middle cerebral artery occlusion (MCAO), it prevented transient depolarizations from progressing to terminal depolarizations and

reduced infarct volumes. Thus halothane showed protective properties in studies of experimental brain ischemia.

Saito et al. teaches on page 2 of 12, that the cats treated with halothane were given halothane before, during and after the MCAO (up to 16 hours).

Saito et al. teach, on page 9 of 12, that one explanation of the ameliorative effects of halothane may be due to reduction of ischemia-induced glutamate accumulation similar to that seen with isoflurane. The decreased ischemic glutamate elevation by halothane (or isoflurane) could be responsible for the reduction of SD-like depolarazations and for infarct volume reduction.

Saito et al. do not teach parenteral administration of a halogenated volatile anesthetic, with an emulsification adjuvant and an emulsifier.

Gray et al. teach, in the abstract, an injectable anesthetic formulation comprising a halogenated anesthetic compound (such as halothane or isoflurane) and at least one emulsifier. On page 3 of the publication, Gray et al. teach that the formulations can include an emulsification adjuvant such as soybean oil and an emulsifier such as lecithin. Additional emulsifiers include polyoxypropylene/polyoxyethylene block co-polymers. Glycerol may be added as a tonicifier.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a volatile halogenated anesthetic in a the method of treating ischemia as Saito et al. teach that halothane and isoflurane (two volatile halogenated anesthetics) have shown protective effects in experimental ischemia. Further it would have been obvious to administer the volatile halogenated anesthetics

parenterally as Gray et al. teach that volatile halogenated anesthetics including halothane and isoflurane can be administered such when using an emulsifier and an emulsifier adjuvant. It is considered routine optimization to discover the optimum concentration of the anesthetic for use in such a method. Further as the compositions have been shown to be suitable for injectable administration it would be routine experimentation to adapt such into a continuous infusion formulation.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

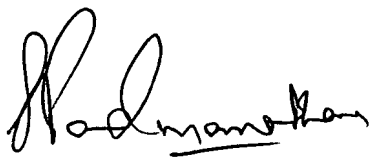
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leonard M. Williams whose telephone number is 571-272-0685. The examiner can normally be reached on MF 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LMW



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SUPERVISORY PATENT EXAMINER